PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 110550:GBC:LK:kf/kw	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. **PCT/AU2004/000089**	International filing date *(day/month/year)* 22 January 2004	Priority date *(day/month/year)* 22 January 2003
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] A61N 2/10		
Applicant SIRTEX MEDICAL LIMITED et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 3 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. [X] *(sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      - [X] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      - [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

[X]	Box No. I	Basis of the report
[ ]	Box No. II	Priority
[ ]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[ ]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[ ]	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
22 November 2004	13 April 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **DR. A TESSEMA** Telephone No. (02) 6283 2271

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/000089

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1 (b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1-25** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☒ the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **26-30** received by this Authority on **22 November 2004** with the letter of 22 November 2004
pages* received by this Authority on with the letter of

☒ the drawings:

pages 1/7-7/7 as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages
☐ the claims, Nos.
☐ the drawings, sheets/figs
☐ the sequence listing (*specify*):
☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		**YES**
	Claims	**1-34**	**NO**
Inventive step (IS)	Claims		**YES**
	Claims	**1-34**	**NO**
Industrial applicability (IA)	Claims	**1-34**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

NOVELTY: INVENTIVE STEP: Claims 1-34

D1. Pouliquen, Daniel, " Magnetite-Dextran Nanocapsules: Preparations and Properties ", Microspheres, Microcapsules & Liposomes (2001), 3 (Radiolabeled and Magnetic Particulates in Medicine & Biology), pages 495-523

The invention defined in claims 1-34 is fully disclosed by D1 (see whole document). D1 discloses magnetic microcapsules composed of iron oxide (magnetite or maghemite – nanomagnetic particles) dispersed in polymeric matrix such as dextran; the iron oxide can initially be coated with dextran and then dispersed in the matrix (dextran). The size (80-200 nm) of the magnetic microcapsules falls within the range-defined in present claims (see, for example, Table 1 at page 499, Names/Codes AMI-25, MSM & DM; page 502, first paragraph; page 505, last paragraph); similarly, the volume fraction (27%-60%) of the nanomagnetic particles of D1 also falls within the range defined in present claims (see, for example, page 495; page 502, first paragraph; page 507, second paragraph). Therefore, D1 fully discloses the invention defined in present claims 1-7, 9, 11-27 and 33. D1 also indicates that the magnetic particles are used as contrast agents in MRI and other biomedical applications such as magnetic hyperthermia (see, for example, page 495); hence, the invention defined in present claims 28-32 and 34 is also fully disclosed by D1. D1 does not specifically indicate the density and/or VAR of the magnetic microparticles defined in present claims 8 and 10, respectively; however, the magnetic microcapsules of D1 are expected to inherently possess these properties because the types of nanomagnetic particles (iron oxide), their sizes and matrices (polymer) of D1 and the claimed invention are the same. It should be noted that present claims are not restricted to microparticles that satisfy all the three properties (VAR, size & density); as drafted, the microparticles are required to satisfy only one of the three properties. It should also be noted that present claims include coated or uncoated nanomagnetic particles dispersed in a matrix/polymeric matrix, as is the case in D1. Therefore, present claims 1-34 are considered not to satisfy the PCT requirements of novelty and inventive step in the light of D1.

The Claims Defining the Invention are as Follows

1. A microparticle composition comprising nanomagnetic particles distributed within a matrix, wherein the microparticles within the composition have a least one of the following properties: (a) a VAR of at least about 1 Watts/cm^3 under alternating magnetic field conditions suitable for use in a patient; (b) a density of about 2.7 or less; or (c) a size range of about 100 nm to about 200 microns.

2. A microparticle composition comprising nanomagnetic particles distributed within a matrix, wherein up to 40% of the volume of each microparticle composition is occupied by the constituent magnetic nanoparticles and the microparticles within the composition have at least one of the following properties: (a) a VAR of at least about 10 Watts/cm^3 under alternating magentic field conditions suitable for use in a patient; (b) a density of about 2.7 or less; or (c) a size range of about 100 nm to 200 microns..

3. A microparticle composition according to claim 2 wherein the volume fraction of nanomagnetic particles in the microparticles is less than 30% of the microparticle composition.

4. A microparticle composition according to claim 2 wherein the volume fraction of nanomagnetic particles in the microparticles is less than 20% of the microparticle composition.

5. A microparticle composition according to claim 2 wherein the volume fraction of nanomagnetic particles in the microparticles is less than 15% of the microparticle composition.

6. A microparticle composition according to claim 2 wherein the volume fraction of nanomagnetic particles in the microparticles is less than 10% of the microparticle composition.

7. A microparticle composition according to claim 2 wherein the volume fraction of nanomagnetic particles in the microparticles is less than 5% of the microparticle composition.

8. A microparticle composition according to any one of claims 1 to 7 wherein the microparticles within the composition have a density of about 2.7 or less.

9. A microparticle composition according to anyone of claims 1 to 8 wherein the microparticles within the composition have a size of about 100 nm to about 200 microns.

10. A microparticle composition according to anyone of claims 1 to 9 wherein the microparticles within the composition have a VAR of about 10 Watts/cm^3 under alternating magnetic field conditions suitable for use in a patient.

11. A microparticle composition according to any one of claims 1 to 10 wherein the alternating magnetic field is operated at a frequency in the range of about 50-300 kHz and field strength of about 60-120 Oe.

12. A microparticle composition according to any one of claims 1 to 10 wherein the alternating magnetic field is operated at a frequency in the range of about 100-200 kHz and field strength of about 60 Oe.

13. A microparticle composition according to claim 11 wherein the alternating magnetic field is operated at a frequency in the range of about 100 kHz and field strength of about 90 Oe.

14. A microparticle composition according to anyone of claims 1 to 13 wherein the nanomagnetic particles distributed within the microparticles are superparamagnetic particles.

15. A microparticle composition according to claim 14 wherein the superparamagnetic particles are either: (a) ferrites of general formula $MO.Fe_2O_3$ where M is a bivalent metal such as Fe, Co, Ni, Mn, Be, Mg, Ca,

Ba, Sr, Cu, Zn, Pt or mixtures thereof, or (b) magnetoplumbite type oxides of the general formula $MO.6Fe_2O_3$ where M is a large bivalent ion, metallic iron, cobalt or nickel.

16.A microparticle composition according to claim 15 wherein the superparamagnetic particles are free Fe, Ni, Cr or Co; oxides of Fe, Ni, Cr or Co; or mixtures of Fe, Ni, Cr or Co.

17.A microparticle composition according to claim 15 wherein the superparamagnetic particles are prepared from iron oxide such as magnetite (Fe_3O_4) or maghemite (γ–Fe_2O_3) and have asize of less than 50 nm.

18.A microparticle composition according to claim 16 wherein the superparamagnetic particles are maghemite nanoparticles.

19.A microparticle composition according to anyone of claims 14 to 18 wherein the superparamagnetic particles have a size of between 1nm and 40nm.

20.A microparticle composition according to any one of claims 1 to 19 wherein the composition is prepared from materials suitable for use in a patient and the particles when delivered to a patient are and placed in an alternating magnetic field are capable of heating tissue in said patient.

21.A microparticle composition according to any one of claims 1 to 19 wherein the matrix in which the nanoparticles are distributed is a polymer matrix.

22.A microparticle composition according claim 21 wherein the polymer matrix is suitable for use in human.

23.A microparticle composition according to either claims 21 or 22 wherein the polymer matrix is a biodegradable polymer matrix.

24.A microparticle composition according to claim 23 wherein the polymer matrix biodegrades to after one to three months following introduction into a patient.

25.A microparticle composition according to anyone of claims 1 to 24 wherein the microparticles in the composition are adapted for site specific delivery to or accumulation within a tissue in a patient.

26.A microparticle composition according to anyone of claims 1 to 25 wherein the composition includes pharmaceutically acceptable carriers and or diluents.

27.A microparticle composition according to anyone of claims 1 to 26 wherein the microparticles in the composition also include bioactive, chemical or radioactive agents that are capable of delivering a therapeutic effect to a patient.

28.A method for heating a target site in a patient including the steps of:

(i) administering a microparticle composition according to any one of claims 22 to 27 to a target site in a patient; and

(ii) exposing the target site to an alternating magnetic field, of a clinically acceptable frequency and strength,

wherein the combination of the alternating magnetic field with the microparticle composition induces heat within the target site.

29.The method according to claim 28 wherein the microparticles are of a size and density that permits the transport of the microparticle composition to the capillary beds supplying the target site.

30.The method according to claim 28 wherein the alternating magnetic field is operated at a frequency in the range of about 50-300 kHz and field strength of about 60-120 Oe.

31.The method according to claim 30 wherein the alternating magentic field is operated at a frequency of about 100 kHz and a field strength of about 90 Oe.

32. The use of a microparticle composition according to any one of claims 1 to 27 in the manufacture of a medicament for the treatment of diseased tissue.

33. A microparticle preparation comprising nanomagnetic particles distributed within a matrix, wherein the microparticles within the preparation have at least one of the following properties: (a) a VAR of at least about 1 Watts/cm3 under alternating magnetic field conditions suitable for use in a patient; (b) a density of about 2.7 or less; or (c) a size range of about 100 nm to about 200 microns.

34. The use of a microparticle preparation according to claim 33 in the manufacture of a medicament for the treatment of diseased tissue.